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TRANSMITTAL FORM

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Application Number	09/297,648
Filing Date	March 10, 2000
First Named Inventor	WILLIAMS, LEWIS T.
Group Art Unit	1631
Examiner Name	BRUSCA, JOHN S.
Attorney Docket Number	2300-1481

ENCLOSURES (check all that apply)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Documents
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below):*
  1. Copy of Notification of Non-Compliance
  2. Response to Notification of Non-Compliance
  3. Copy of Brief on Appeal in triplicate
  4. Copy of Somerville Declaration in triplicate
  5. Postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	JAMES S. KEDDIE, PH.D., 48,920 BOZICEVIC, FIELD & FRANCIS LLP
Signature	James S Keddie
Date	March 5, 2004

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RESPONSE TO NOTIFICATION OF NON-COMPLIANCE Address to: Box Assistant Commissioner for Patents Washington, D.C. 20231	Attorney Docket Confirmation No.	2300-1481 1096
	First Named Inventor	Lewis T. Williams
	Application Number	09/297,648
	Filing Date	March 10, 2000
	Group Art Unit	1631
	Examiner Name	John S. Brusca
	Title	"Novel Human Genes and Gene Expression Products II"

Sir:

This communication is responsive to the Notification of Non-Compliance dated February 12, 2004, for which a one month period for response was given making this response due on or before March 12, 2004.

In the above-referenced Notification, the Office stated that the Appeal Brief filed on December 11, 2003 is defective for failure to comply with one or more provisions of 37 C.F.R. § 1.192(c).

The Applicants file herewith, in triplicate, a complete substitute Appeal Brief within the time period allowed. The Applicants respectfully submit that the substitute Appeal Brief meets the requirements of 37 C.F.R. § 1.192(c).

The fees associated with this Appeal Brief have already been paid. Because of this, no further fees should necessary. However, if any further fees are required, the Commissioner is hereby authorized to charge Deposit Account No. 50-0815, order number 2300-1481.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: March 5, 2004

By: James S Keddie
James S. Keddie
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,648	03/10/2000	LEWIS T. WILLIAMS	2300-1481CIP	1096

27476 7590 02/12/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED: 02/12/2004

OIPE JC160 MAR 05 2004 PATENT & TRADEMARK OFFICE

FEB 2004 Received Chiron Corporation Intellectual Property

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETED
Appeal Brief 03/12/04
LD 08/12/04

DOCKETED on/by 2/17/04
Atty. CAL PA
File # PP01481.002
Due Date 3/13/04 Ext RS5
Final Date 8/13/04 RSP
12/11/03 Brief is defective

PTO-90C (Rev. 10/03)

Notification of Non-Compliance With 37 CFR 1.192(c)

Application No.	Applicant(s)
09/297,648	STACHE-CRAIN ET AL.
Examiner	**Art Unit**
John S. Brusca	1631

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

The Appeal Brief filed on *11 December 2003* is defective for failure to comply with one or more provisions of 37 CFR 1.192(c). See MPEP § 1206.

To avoid dismissal of the appeal, applicant must file IN TRIPLICATE a complete new brief in compliance with 37 CFR 1.192(c) within the longest of any of the following three **TIME PERIODS**: (1) **ONE MONTH or THIRTY DAYS** from the mailing date of this Notification, whichever is longer; (2) **TWO MONTHS** from the date of the notice of appeal; or (3) within the period for reply to the action from which this appeal was taken. **EXTENSIONS OF THESE TIME PERIODS MAY BE GRANTED UNDER 37 CFR 1.136.**

1. ☐ The brief does not contain the items required under 37 CFR 1.192(c), or the items are not under the proper heading or in the proper order.

2. ☐ The brief does not contain a statement of the status of all claims, pending or cancelled, or does not identify the appealed claims (37 CFR 1.192(c)(3)).

3. ☐ At least one amendment has been filed subsequent to the final rejection, and the brief does not contain a statement of the status of each such amendment (37 CFR 1.192(c)(4)).

4. ☒ The brief does not contain a concise explanation of the claimed invention, referring to the specification by page and line number and to the drawing, if any, by reference characters (37 CFR 1.192(c)(5)).

5. ☒ The brief does not contain a concise statement of the issues presented for review (37 CFR 1.192(c)(6)).

6. ☐ A single ground of rejection has been applied to two or more claims in this application, and

   (a) ☐ the brief omits the statement required by 37 CFR 1.192(c)(7) that one or more claims do not stand or fall together, yet presents arguments in support thereof in the argument section of the brief.

   (b) ☐ the brief includes the statement required by 37 CFR 1.192(c)(7) that one or more claims do not stand or fall together, yet does not present arguments in support thereof in the argument section of the brief.

7. ☐ The brief does not present an argument under a separate heading for each issue on appeal (37 CFR 1.192(c)(8)).

8. ☐ The brief does not contain a correct copy of the appealed claims as an appendix thereto (37 CFR 1.192(c)(9)).

9. ☒ Other (including any explanation in support of the above items):

The statement of issues does not discuss the single ground of rejection specifically and does not state which claims are rejected under the single ground of rejection.
The grouping of claims is not limited to the single ground of rejection.

John S. Brusca
Primary Examiner
Art Unit: 1631

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of	)	
	)	Group Art Unit: 1631
Williams *et al.*	)	
	)	Examiner: John S. Brusca
Serial No. 09/297,648	)	
	)	Atty. Docket No. 2300-1481
Filed: March 10, 2000	)	PP-1481-002

For: **HUMAN GENES AND GENE EXPRESSION PRODUCTS II**

BRIEF ON APPEAL

James S. Keddie
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of	)	
	)	Group Art Unit: 1631
Williams *et al.*	)	
	)	Examiner: John S. Brusca
Serial No. 09/297,648	)	
	)	Atty. Docket No. 2300-1481
Filed: March 10, 2000	)	PP-1481-002

For: **HUMAN GENES AND GENE EXPRESSION PRODUCTS II**

BRIEF ON APPEAL

Commissioner of Patents
Alexandria, V.A. 20231

Sir:

Appellants submit an original and two copies of this brief. Appellants file the Notice of Appeal herewith.

Please charge the $330.00 fee for filing this Brief, the $290.00 for the Request for Oral Hearing and the Notice of Appeal fee of $330.00 to our Deposit Account No. 50-0815, order number 2300-1481. If this fee is incorrect, please charge or credit the account accordingly.

REAL PARTIES IN INTEREST

The real parties in interest in this application are Chiron Corporation and Hyseq Corporation to which this application is assigned. Hyseq Corporation has changed its name to Nuvelo, Inc.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

RELATED PATENTS AND APPLICATIONS

The above referenced application is a 35 USC § 371 national phase application of PCT application serial number PCT/US99/01619, filed December 28, 1999, which application claims the benefit of the following provisional patent applications: 60/072,910, filed January 28, 1998, 60/075,954 filed February 24, 1998, 60/080,114 filed March 31, 1998, 60/080,515 filed April 3, 1998, 60/105,234 filed October 21, 1998, 60/105,877 filed October 27, 1998 and 60/080,666 filed April 3, 1998.

STATUS OF CLAIMS

Claims 146-154 stand rejected. Claims 146-154 are appealed.

STATUS OF AMENDMENTS

The last amendment to the claims was filed November 1, 2002. That amendment has been entered.

Appendix I sets forth the currently pending claims.

SUMMARY OF THE INVENTION

All of the claims are directed to polynucleotide molecules having at least a 50 contiguous nucleotides of the sequence set forth in SEQ ID NO:253 (page 1 lines 28-31, page 9, lines 7-10), which polynucleotides may be used to detect nucleic acids that are expressed at higher levels in cancerous cells as compared to non-cancerous cells (page 3, lines 23-28, page 43, lines 15-25). The claimed polynucleotides are therefore useful for a wide variety of diagnostic purposes.

Claim 146 is illustrative of the claims on appeal:

146. An isolated polynucleotide comprising at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 and the complement thereof.

Claims 147-154, recite vectors and host cells (page 3, lines 3-6), polynucleotides that hybridize (page 6, lines 1-3), polynucleotides deposited with the A.T.C.C. (page 131, lines 13-15) and nucleic acid products made by amplification (page 9 lines 3-6), that directly or indirectly, recite the defining characteristics of Appellants' invention: a polynucleotide having at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 and the complement thereof.

ISSUES

All of the pending claims (claims 146-154) are rejected for assertedly not satisfying the written description requirement of 35 U.S.C. § 112, ¶1. Specifically, all pending claims are rejected for encompassing polynucleotides having a sequence longer than the polynucleotide sequence recited in the claim (i.e., 50 contiguous nucleotides of SEQ ID NO:253). The Examiner argues that these longer sequence are not adequately described in the '648 specification, and,

accordingly, claims encompassing the longer sequences are rejected for not satisfying the written description requirement of 35 U.S.C. § 112, ¶1. The Appellants disagree.

Accordingly, the issue on appeal is:

I. WHETHER THE APPEALED CLAIMS ARE PROPERLY REJECTED AS NOT BEING ADEQUATELY DESCRIBED BY THE '648 SPECIFICATION UNDER A WRITTEN DESCRIPTION REQUIREMENT OF 35 U.S.C. §112, FIRST PARAGRAPH.

GROUPING OF CLAIMS

The following groups of claims stand or fall together with respect to issue I:

Group I: Claims 146-150 and 152-154

Group II: Claim 151

SUMMARY OF ARGUMENT

Each of the appealed claims is directed to a genus of polynucleotides molecules that is defined by the required presence of an identifying polynucleotide sequence of at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 or of at least 50 contiguous nucleotides of an insert contained in a vector deposited at the A.T.C.C., and the complements thereof, as discovered by the inventors. The identifying polynucleotide sequence is recited either directly or indirectly in all of the claims. None of the claims requires that the claimed polynucleotide molecules encode a "full-length cDNA", and none of the claims requires that the claimed polynucleotides encode a particular amino acid sequence.

The utility of the claimed nucleic acids (for example, as cancer diagnostic probes or starting materials for such probes) has not been disputed and has never been challenged.

All of the appealed claims are written in open form. That is, they employ the claim transition phrase "comprising." Again, claim 146 is illustrative (see Summary of the Invention, *supra*). As such, any of the nucleic acids encompassed by the appealed claims may contain nucleic acid residues flanking the 5' and/or the 3' ends of the recited identifying polynucleotide sequence. The appealed claims do not recite the sequence or function of the flanking nucleic acids, and do not recite that the flanking nucleic acids encode a portion of a protein. It is this open form of the claims that appears to have given rise to all rejections on appeal.

Each appealed claim stands rejected under 35 U.S.C. § 112, ¶1, assertedly because the specification of the '648 patent application does not adequately describe the claimed invention.

Since the exact nucleotide sequence of SEQ ID NO:253 is provided in the specification of the '648 patent application, the Appellants have repeatedly questioned the support underlying the Office's rejection of the pending claims and have requested an Examiner's affidavit under 37 C.F.R. § 1.104(d)(2). No support, however, has been provided. Instead, the Office has stated that that the appealed claims, because they are written in open form, encompass the full-length cDNA to which SEQ ID NO:253 corresponds, and, because the sequence of that full-length cDNA is not specifically disclosed in the specification, the claims do not meet the written description requirement of 35 U.S.C. § 112, ¶1. In other words, the Examiner has taken the position that unless Appellants disclose the polynucleotide sequence of a single species, i.e., the "full-length cDNA", the specification fails to meet the written description requirement of 35 U.S.C. §112, ¶1.

Appellants agree that a full-length cDNA having the sequence of SEQ ID NO:253 is encompassed by the appealed claims. There is, however no limitation in any of the claims that requires that the claimed polynucleotides be the full length cDNA. In other words, while the full-length cDNA to which SEQ ID NO:253 corresponds is encompassed by the claims, the claims

are not so limited to such cDNAs. Rather, the full-length cDNA is but one species of the polynucleotides encompassed by the claimed genus. Since there is no requirement that every species of a claimed genus be specifically described in a patent specification in order to satisfy 35 U.S.C. §112, ¶1, there is no basis for this rejection.

Moreover, because there is no indication in the record that the full-length cDNA to which SEQ ID NO:253 was known in the art when the '648 specification was filed, the full-length cDNA to which SEQ ID NO:253 corresponds constitutes a later-discovered species within Appellants' generic claims. The fact that Appellants' generic claims encompass a species which is not recited in the claims is irrelevant as to whether Appellants are entitled to the appealed claims. What is relevant is whether the appealed generic claims, as properly interpreted, meet the statutory requirements for written description under 35 U.S.C. § 112, ¶1. Appellants believe that all the claims meet these statutory requirements and that the rejections are based on an improper application of the law and should be withdrawn.

ARGUMENT

I. The 1952 Patent Act Does Not Provide a Test for Written Description Apart From Enablement and/or the Heightened Tests Set Forth in *Lilly*

The rejection for failure to comply with the written description requirement should be reversed because the 1952 Patent Act does not contain a separate written description requirement apart from enablement under 35 U.S.C. § 112, ¶1 and the prohibition against new matter under 35 U.S.C. § 132. Furthermore, even if there is a separate written description requirement in § 112, ¶1, the elevation of that test beyond the requirements of enablement and the prohibition against new matter is contrary to binding precedent of the Court of Customs and Patent Appeals (C.C.P.A.) and the Court of Appeals of the Federal Circuit. *See, e.g., Enzo Biochem. Inc. v. Gen-*

Probe Inc, 63 U.S.P.Q.2d (BNA) 1609, 1622 (Fed. Cir. 2002) (Rader, J. dissenting). A later three-judge panel cannot overturn prior precedential decisions of the C.C.P.A. and the Court of Appeals of the Federal Circuit. *Enzo Biochem. Inc. v. Gen-Probe Inc*, 63 U.S.P.Q.2d (BNA) 1609, 1628; *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). Thus, because *University of California v. Eli Lilly and Co.*,119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), purports to change or elevate the written description requirement inconsistent with prior binding precedent and beyond the requirements of enablement under § 112, ¶1 and the prohibition against new matter under § 132, the Office should not apply it in the examination of applications. In other words, because the rejection of claims 146-154 was primarily based on *Lilly*, the rejection should be reversed.

Appellants note that the discussions of *Lilly* in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 2003 U.S. App. LEXIS 118, 65 U.S.P.Q.2D (BNA) 1385 (Fed. Cir. 2003) and in *Moba v. Diamond Automation*, 2003 U.S. App. LEXIS 6285 (Fed. Cir. 2003), indicate that the application of the tests for written description as set out in *Lilly* is currently in question. Appellants appreciate that the Board may feel that this issue should be left to the Federal Circuit to review. Nevertheless, Appellants want to provide the Board with an opportunity to express its views for the benefit of further review, as well as to preserve the issue for appeal.

II. The Specification Contains a Written Description of the Invention According to 35 U.S.C. § 112, ¶1

Whether a patent specification meets the written description requirement for a claimed invention is a question of fact. *Vas-Cath,* 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1116. In arguing that they have met the written description requirement, Appellants have provided the U.S. Patent and Trademark Office with an extensive factual record. That record,

which includes the expert declaration of Dr. Christopher R. Somerville, filed November 1, 2002, establishes beyond doubt that all the appealed claims meet the written description requirement of 35 U.S.C. § 112, ¶1. The Office has improperly ignored and discounted Appellants' factual showing and has instead made unsupported assertions in making the rejection. Appellants have repeatedly questioned the support underlying the Examiner's rejection and have requested an Examiner's affidavit under 37 C.F.R. § 1.104(d)(2). No such support, however, has been provided. Thus, there is no evidentiary basis for the Examiner's alleged factual finding. In addition, the Examiner has misstated and misapplied the law on written description. The rejection should be reversed.

A. The Legal Standards for Written Description

The rejection is based on an allegation that because the claims are written in open form using the transitional phrase "comprising", the scope of the written description provided by the specification is insufficient to support the claims.

The first paragraph of 35 U.S.C. § 112 requires that the specification provide a written description of the claimed invention:

> [t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The purpose of the written description requirement is to ensure that the specification conveys to those skilled in the art that the applicants possessed the claimed subject matter as of the filing date sought. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). *See also All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 2002 U.S. App. LEXIS 22372, *10-11 (Fed. Cir. 2002) ("the specification must simply indicate to

persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed."). Thus, the test for whether a claimed invention is adequately described has often been stated as whether or not one of skill in the art would have understood from the specification that an applicant possessed the claimed subject matter when the specification was filed. *See, e.g., Ralston Purina Co. v. Far-Mar-Co,* 772 F.2d 1570, 1575, 227 U.S.P.Q. (BNA) 177, 179 (Fed. Cir. 1985). Whether the specification meets the written description requirement for the claimed invention is a question of fact. *Vas-Cath,* 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1116.

The specification must be considered as a whole when determining whether the written description requirement is met. *In re Wright*, 866 F.2d 422, 425, 9 U.S.P.Q.2d (BNA) 1649, 1651 (Fed. Cir. 1989). Compliance with the written description requirement must be assessed on a case-by-case basis. *Crown Operations International, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1376, 62 U.S.P.Q.2d (BNA) 1917, 1922 (Fed. Cir. 2002).

What is required to satisfy the written description requirement depends on the nature of the invention claimed. *In re Di Leone*, 436 F.2d 1404, 1405, 168 U.S.P.Q. (BNA) 592, 593 (C.C.P.A. 1971). According to *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 63 U.S.P.Q.2d (BNA) 1609 (Fed. Cir. 2002), "the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed." 296 F.3d 1316, 1326, 63 U.S.P.Q.2d (BNA) 1609, 1615. Specifically discussing nucleic acid molecules, the *Enzo* court recently approved two means by which the written description requirement can be met. First, "reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply

with the written description requirement of § 112, ¶ 1." 296 F.3d 1316, 1325, 63 U.S.P.Q.2d (BNA) 1609, 1613. Second, the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Written Description Guidelines, 66 Fed. Reg. 1099, 1106 (January 5, 2001); approved in *Enzo*, 296 F.3d 1316, 1325, 63 U.S.P.Q.2d (BNA) 1609, 1613.

The Court of Appeals for the Federal Circuit also has stated that written description of a genus of polynucleotide molecules may be achieved by sufficiently describing a representative number of species within the genus:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. This is analogous to enablement of a genus under § 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

University of California v. Eli Lilly and Co., 119 F.3d 1559, 1569, 43 U.S.P.Q.2d (BNA) 1398, 1406 (Fed. Cir. 1997) (footnotes and internal references omitted). As long as the specification permits one of skill in the art to "visualize or recognize the identity of members of the genus," the genus is adequately described. 119 F.3d 1559, 1568, 43 U.S.P.Q.2d (BNA) at 1406. The options set forth in *Lilly* for describing a genus of polynucleotide molecules are reflected in the U.S. Patent and Trademark Office's Written Description Guidelines:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to

> drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics . . . .

66 Fed. Reg. at 1106. As noted above, the Court of Appeals for the Federal Circuit has specifically approved this option for satisfaction of the written description requirement. *Enzo*, 296 F.3d at 1325, 63 U.S.P.Q.2d (BNA) 1613.

However, it is also noted that Lilly fails as a test for adequate written description in several cases, e.g., *Amgen Inc. v. Hoechst Marion Roussel, Inc.* 314 F.3d 1313, 2003 U.S. App. LEXIS 118, 42, 65 U.S.P.Q.2D (BNA) 1385 (Fed. Cir. 2003) (stating that "Both Eli Lilly and Enzo Biochem are inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend."). In particular, the Federal Circuit in *Moba v. Diamond Automation, Inc.*, 2003 U.S. App. LEXIS 6285, 33 (Fed. Cir. 2003) stated: "the Lilly disclosure rule does not require a particular form of disclosure because one of skill could determine from the specification that the inventor possessed the invention at the time of filing". Despite the uncertainty in the law regarding the application of the structural test set forth in *Lilly*, it is this test that nonetheless forms the primary basis for this rejection.

Structural tests for adequate written description of a DNA invention that are similar to the test provided by *Lilly* are also provided in *Fiddes v. Baird* 30 U.S.P.Q.2d 1481, 1398 (BPAI 1993):

> An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.
>
> * * *

> If a conception of a DNA requires a specific definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity....[O]ne cannot describe what one has not conceived. (*Id.* at 1482-83, *citing Fiers,* 984 F.2d at 1170-71.)

and in *Amgen, Inc. v. Chugai Pharmaceutical, Co*, 927 F.2d 1200, 18 U.S.P.Q.2d (BNA) 1016 (Fed. Cir. 1991). The *Amgen* court stated:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. (*Amgen,* 927 F.2d at 1206, citations omitted)

As such, Amgen provides a test for adequate written description that involves allowing sufficiently distinguishing a claimed compound from other compounds.

Even in an "unpredictable art," applicants "are *not* required to disclose *every* species encompassed by their claims . . . ." *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. (BNA) 214, 218, (C.C.P.A. 1976). Thus, features that apply to only some species within a generic claim – but not to all species encompassed by the claim – need not be described to satisfy the written description requirement. Otherwise, to claim a genus, every species within a genus would have to be explicitly described. That is not the law. *See Engel Indus., Inc. v. Lockformer Co.*, 946 F.2d 1528, 1531, 20 U.S.P.Q.2d (BNA) 1300, 1302 (Fed. Cir. 1991) ("Unclaimed subject matter is not subject to the disclosure requirements of § 112; the reasons are pragmatic: the disclosure would be boundless, and the pitfalls endless."). *See also Phillips Petroleum v. U.S. Steel Corp.*, 673 F. Supp. 1278, 1292, 6 U.S.P.Q.2d (BNA) 1065, 1074 (D. Del. 1987) ("The applicant is not required to include in his application support for matters not set forth in the claim."), *aff'd* 865

F.2d 1247, 9 U.S.P.Q.2d (BNA) 1461 (Fed. Cir. 1989). Description of later-invented species that now fall within a claimed genus certainly is not required. *Rexnord Corporation v. Laitram Corporation*, 274 F.3d 1336, 1344, 60 U.S.P.Q.2d (BNA) 1851, 1856 (Fed. Cir. 2001) ("Our case law is clear that an applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention."). *See also In re Hogan and Banks*, 559 F.2d 595, 605-06, 194 U.S.P.Q. (BNA) 527, 537 (C.C.P.A. 1977); *United States Steel Corporation v. Phillips Petroleum Company*, 865 F.2d 1247, 1251-52, 9 U.S.P.Q.2d (BNA) 1461, 1465 (Fed. Cir. 1989).

B. Grouping of claims

The claims are grouped as follows:

Group I claims (claims 146-150 and 152-154). The polynucleotides of Group I have a defining feature of a polynucleotide sequence of at least 50 contiguous nucleotides of SEQ ID NO:253, or complement thereof.

Group II claim (claim 151). The polynucleotides of Group II have a defining feature of a polynucleotide sequence of at least 50 contiguous nucleotides of an insert of a vector deposited at the American Type Culture Collection (A.T.C.C.).

C. Appellants Have Provided Overwhelming and Unrebutted Factual Evidence for the Legal Conclusion that the Specification Sufficiently Describes Claims 146-154.

As noted above, the question of whether a patent specification meets the written description requirement for a claimed invention is a question of fact. Vas-Cath, 935 F.2d at 1563, 19 U.S.P.Q.2d (BNA) at 1116. In order to answer this question, the Appellants provided during prosecution of this case an expert declaration of Dr. Christopher Somerville and accompanying

documentary exhibits filed November 1, 2002 ("SD"). A copy of Dr. Somerville's declaration is enclosed herewith as Appendix II.

Dr Somerville is a Director of the Carnegie Institution of Washington Department of Plant Biology, a Professor of the Department of Biological Sciences at Stanford University, an elected member of the U.S. National Academy of Sciences, an elected fellow of the Royal Societies of London and Canada and has served on the editorial boards of several international peer-reviewed journals and several government panels. SD ¶ 3. Dr. Somerville has worked in the field of recombinant DNA technology for over 20 years and has published over 150 articles in the fields of genetics, biochemistry, molecular biology and genomics. SD ¶ 3.

Dr. Somerville understands that the '648 application is to be viewed from the standpoint of one of ordinary skill in the art in the relevant field at the time of filing of the application (referred to by Dr. Somerville and by the Appellants as a "Skilled Person"). SD ¶ 7. Dr. Somerville believes that he is qualified by training and experience to address what a Skilled Person would have understood from a reading of the specification of U.S. Patent Application No. 09/297,648 as of its filing date on March 10, 2000. SD ¶ 9

Dr. Somerville has reviewed the above referenced patent application and the Office Action , SD ¶ 4. Dr. Somerville understands that the polynucleotides encompassed by each of the claims are a genus of polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 50 contiguous nucleotides of SEQ ID NO:253 or at least 50 contiguous nucleotides of an insert of a vector deposited with the A.T.C.C.. SD ¶ 5. Dr. Somerville also understands that the word "comprising" as used in the appealed claims means that flanking sequences can be present in addition to a recited sequence. SD ¶ 12.

Dr. Somerville stated that it is his unequivocal opinion that a Skilled Person would conclude from a review of the '648 application as a whole, that the Inventions (i.e., the subject matter defined by claims 146-154) were described in the '648 application and in the inventors' possession, and further that the disclosure of '648 application contains representative examples of the Inventions. SD ¶ 8.

When read in conjunction with the '648 specification, it is Dr. Somerville's unequivocal opinion that, a Skilled Person would find that the '648 specification describes polynucleotides fully representative of the genus of polynucleotides of the Invention since:

a) the Skilled Person would recognize disclosure of SEQ ID NO:253 as fully representative of the genus of the Invention since it is a complete disclosure of the common structural feature (i.e., at least 50 contiguous nucleotides of SEQ ID NO:253) of the Inventions; and

b) the Skilled Person would recognize the vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics. SD ¶ 18.

The bases for this conclusion are set forth below.

1. Skilled person

A Skilled Person in the field of recombinant DNA technology in March 2000 is represented by a scientist with a Ph.D. degree and two years of post-doctoral training. SD ¶ 7. A Skilled Person would have the ability to analyze a DNA sequence using the common general knowledge, tools, and methods available in the field and without inventive effort. *Id.* Furthermore, such a Skilled Person would have had access to and would have used as needed

persons of ordinary skill in other technical fields, such as (by way of illustration and not limitation) cellular biology, oncology, biochemistry, immunology, physiology and diagnostics. *Id.*

In March 2000, the common general knowledge, tools, and well-known methods available in this field were extensive. SD ¶ 8. Widely available methods included nucleotide hybridization, nucleic acid cloning, polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), gene sequencing and cDNA library construction and screening. *Id.* In addition, several "bioinformatics" tools were available, such as bioinformatics programs for searching a database of nucleic acids sequences for similar nucleic acid sequences (e.g. BLAST), programs for comparing two nucleic acid sequence (e.g. the BESTFIT or GAP programs as provided by the University of Wisconsin's GCG program) and programs for predicting and annotating coding sequences of genes (e.g. GENSCAN and XGRAIL). *Id.*

2. Polynucleotide molecules claimed in each of claim Groups I and II contain common structural features.

As discussed above, the polynucleotide molecules encompassed by Group I claims contain a common structural feature that is a sequence of at least 50 contiguous nucleotides of SEQ ID NO:253, or complement thereof. The polynucleotides of the claim of Group II have a common structural feature that is a sequence of at least 50 contiguous nucleotides of an insert of a vector deposited at the A.T.C.C.

3. The '648 specification explicitly describes the common structural feature that the polynucleotide molecules of Group I must contain.

The sequence of SEQ ID NO:253 is provided in the sequence listing of the '648 application. SD ¶ 11. As recited in the sequence listing, SEQ ID NO:253 is provided as follows:

<400> 253
gaacaaagaa ggaatgtctt cctcatgttt gggtctatag aagacgttaa agaaaacttc 60
aagaaagtgg gtttgaggca tgagccacca cgcctggcca aaggatttaa tgaattaatg 120
gatgtacagt gctggggctg ttattctagg gcctgcattg agactcacat tttgccatca 180
aaagcctttt aagaggtgga ggttgcggtg agctgacatg gtgccactgc actccggcct 240
gagtgacaga gtgagactct gtctcacaaa aaaaataatg ccctttaaat aatgaataat 300

Description of polynucleotide molecules containing at least *50* contiguous nucleotides of SEQ ID NO:253 is found on page 9, lines 6-10 of the '648 specification. SD ¶ 11.

Further, the sequence set forth in SEQ ID NO:253 was obtained a plasmid contained in clone number M00001448D:C09, SD ¶ 11, and this clone was deposited with the A.T.C.C.

A Skilled Person, taking these disclosures together, would find specific description in the '648 application of the recited common structural feature for Group I claims: the sequence of at least 50 contiguous nucleotides of SEQ ID NO:253. SD ¶ 11.

4. The '648 specification describes a vast number of polynucleotide molecules that are larger than the common structural feature and contain the common structural feature.

The '648 specification describes nucleic acid probes containing the common structural feature that are often longer than 50 contiguous polynucleotides in length. '648 specification page 9 lines 15-22, page 10 lines 12-19, SD ¶ 13. Sambrook *et al.*, incorporated by reference into the '648 specification, also describes several types of probes that contain flanking sequences, including hybridization probes, oligonucleotide probes, RNA probes, plasmid probes and polymerase chain reaction probes. SD ¶ 13. For example, a skilled person would recognize that a probe may contain polylinker sequences, or an oligonucleotide "tail". SD ¶ 13.

Polynucleotide vectors containing the common structural feature, which a Skilled Person would recognize as always being longer then the common structural feature, are described in several positions of the specification. '648 specification page 10 lines 3-6, page 15 lines 5-12, page 16 lines 16-23, page 74 line 13-page 75 line 19, SD ¶ 14.

The '648 specification also describes cDNA and gene polynucleotide molecules containing the common structural feature, one of which was deposited at the A.T.C.C. '648 specification page 8 lines 16-21, '648 specification page 8 lines 13-page 9 line 2, and SD ¶ 15, SD ¶ 16.

The '648 specification specifically describes a wide variety of polynucleotide molecules containing at least 50 contiguous nucleotides of SEQ ID NO:253 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. SD ¶ 17. As such, the '648 specification describes large polynucleotides containing fragments of SEQ ID NO:253. The vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 and having such flanking sequences. *Id.* The overall disclosure of the specification demonstrates that there is no criticality to sequences flanking the polynucleotides of the Invention. *Id.* Rather, selection of such flanking sequences is an arbitrary matter of design. *Id.* The Skilled Person would readily appreciate from the specification that the sequence of SEQ ID NO:253 can be incorporated within a vast number of larger polynucleotide molecules, and that each of these sequences is identifiable as having at least 50 contiguous nucleotides of SEQ ID NO:253. Each of these polynucleotide molecules is, for example, useful as a probe or a starting material for a probe (see, e.g., page 5, lines 7-14 of the '648 specification). SD ¶ 17.

5. A vector that is fully representative of the claimed polynucleotide molecules was deposited with the A.T.C.C. prior to the filing date of the '648 patent application.

Table 1 of the '648 application describes biological deposits which include vectors containing an insert, which insert contains the sequences described in the application. Table 1 indicates that a clone encompassing the sequence of SEQ ID NO:253 is deposited as clone M00001448D:C09 at the A.T.C.C.. SD ¶ 29. This deposit was made before the filing date of this application.

The Skilled Person would recognize the vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics. SD ¶ 18.

6. A Skilled Person would recognize the common structural feature and be able to straightforwardly determine whether a given polynucleotide falls within any one of the claims based on the provided structural feature

The Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within any one of the claims based on the provided structural characteristics or routine hybridization experiments. SD ¶ 45 Only routine methodologies would be required to determine whether a given polynucleotide would be within a genus of an Invention. *Id.* For example, a Skilled Person, by performing a simple sequence comparison, e.g. a pairwise "BESTFIT" alignment between SEQ ID NO:253 and any given nucleotide would have been able to straightforwardly determine whether a given polynucleotide fell within any one of the claims:

the given polynucleotide either has 50 nucleotides of sequence identity with SEQ ID NO:253 or it does not. SD ¶ 20.

D. The Unrebutted Facts and the Law Mandate Reversal of the Rejection of Claims 146-154 Based on the Written Description Requirement.

1. Properly construed claims 146-154 recite specific sequences but contain no requirement for a full length cDNA.

The first step in a written description inquiry is to properly construe the claims. *Vas-Cath Inc.*, 935 F.2d at 1560, 19 U.S.P.Q.2d (BNA) at 1116.

Group I claims encompass isolated polynucleotide molecules, vectors containing the polynucleotide molecules, and host cells containing the vectors. Each of the claims of Group I recites directly or indirectly, the defining characteristics of Appellants' invention: at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 and the complement thereof

Claim 146 is illustrative of the claims on appeal:

> 146. An isolated polynucleotide comprising at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 and the complement thereof.

The claim of Group II (Claim 151) encompasses a polynucleotide molecule that recites a defining characteristic of the Appellants' invention: at least 50 contiguous nucleotides of either strand of a nucleotide insert contained in a vector deposited as clone M00001448D:C09 of A.T.C.C. Deposit Number 207068. This insert contains the sequence of SEQ ID NO:253.

For Group I claims, the claimed polynucleotides must include at least 50 contiguous nucleotides of SEQ ID NO:253 or its complement. The subject polynucleotide molecules are claimed using an "open" claim structure and thus may include flanking sequences.

For the Group II claim, the claimed polynucleotides must include at least 50 contiguous nucleotides of an insert of a vector deposited with the A.T.C.C. This insert includes a polynucleotide having the sequence of SEQ ID NO:253. Again, the subject polynucleotide molecules are claimed using an "open" claim structure and thus may include flanking sequences.

The claims do not require any particular flanking sequence. In particular, none of the claims requires that the isolated polynucleotides are full length cDNA, have an open reading frame, or have any particular structure or biological function. The Appellants asserted this during prosecution. See, e.g., Amendment and Response filed November 1, 2002, page 8. The Examiner never disputed Appellants' assertion or pointed to any claim term that could possibly be read to impose such a requirement. In fact, the Examiner stated that the structure of flanking vector polynucleotide sequences are well known to one of skill in the art. See the Office Action dated January 15, 203 (paper 32), page 4.

The claimed polynucleotides, including polynucleotides the have flanking sequences, can serve as probes or starting materials for probes in cancer diagnostics SD ¶ 18. As such, every one of the claimed polynucleotides has an acknowledged specific, substantial and credible utility. *Id.* None of these uses requires a claimed polynucleotide be full length cDNA. In fact, none of these uses requires a claimed polynucleotide to contain flanking nucleic acids of any particular sequence. As Dr. Somerville states, the overall disclosure of the specification demonstrates that there is not criticality to sequences flanking the polynucleotides of the Invention. Rather, selection of such flanking sequences is an arbitrary matter of design.

2. The '648 specification satisfies the tests for adequate written description under each of Vas-Cath, Lilly, and Enzo.

Vas-Cath sets forth a test for whether a specification meets the written description requirement. 935 F.2d at 1563-64, 19 U.S.P.Q.2d at 1117. *Lilly* and *Enzo* set forth means by

which a specification can satisfy the written description requirement for generic claims to nucleic acid molecules in particular. *Lilly*, 119 F.3d at 1569, 43 U.S.P.Q.2d at 1406; *Enzo*, 296 F.3d at 1324, 1325, 63 U.S.P.Q.2d at 1613. The extensive factual record in this application demonstrates without question that the '648 specification satisfies the tests for under each of the rubrics of written description enunciated in *Vas-Cath*, *Lilly*, and *Enzo*, and, as such, provides adequate written description of the subject matter encompassed by each of the appealed claims 146-154.

a. *Vas-Cath*

Under *Vas-Cath*, the '648 specification must convey to one of skill in the art that Appellants possessed the invention to which the appealed claims are directed when that specification was filed. 935 F.2d at 1563-64, 19 U.S.P.Q.2d (BNA) at 1117.

Dr. Somerville, in his declaration, understands that the claimed polynucleotides may contain flanking sequences. For each of the appealed claims, Dr. Somerville establishes beyond doubt that the inventors' disclosure meets the possession test provided by Vas-Cath:

Dr. Somerville declares:

> Based on the foregoing, it is also my unequivocal opinion that a Skilled Person would find that the '648 specification demonstrates that applicants had possession of the genera of polynucleotides of claims 146-148. SD ¶ 19
>
> It is therefore my unequivocal opinion that a Skilled Person would, in March 2000, have found the specific description of the claimed genus of polynucleotides in the specification to be a sufficient structural description of the claimed Inventions and to demonstrate applicants had possession of the Invention of Claims 149 or 150. SD ¶ 26
>
> Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claim 151 and recognize that the inventors were in possession of that Invention. SD ¶ 31

> Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claims 152-154 and recognize that the inventors were in possession of that Invention. SD ¶ 41

Dr. Somerville's Declaration contains a sound basis of this conclusion.

First, Dr. Somerville states that the '648 specification explicitly teaches the common structural feature of each of the claimed genera of nucleic acids, *i.e.*, the polynucleotide sequence of SEQ ID NO:253. SD ¶ 11. Dr. Somerville states that a description of polynucleotides containing at least *50* contiguous nucleotides of SEQ ID NO:253 is found on page 9, lines 6-10 of the '648 specification. SD ¶ 11. Dr. Somerville states that a Skilled Person, taking these disclosures together, would find specific description in the '648 application of the recited common structural feature for Group I claims: the sequence of at least 50 contiguous nucleotides of SEQ ID NO:253. SD ¶ 11.

Dr. Somerville explains how the '648 specification specifically describes a wide variety of polynucleotides containing at least 50 contiguous nucleotides of SEQ ID NO:253 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. SD ¶ 17.

Furthermore, an actual clone encompassing the sequence of SEQ ID NO:253 was deposited with the A.T.C.C. as clone number M00001448D:C09 of A.T.C.C. Deposit Number 207068. SD ¶ 11. Dr. Somerville opines that such a deposit is an example of a polynucleotide containing SEQ ID NO:253 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics. SD ¶ 18.

According to Dr. Somerville, the Skilled Person would readily appreciate from the '648 specification that the sequence of SEQ ID NO:253 can be incorporated within a vast number of

larger polynucleotides, and that each of these sequences is identifiable as having at least 50 contiguous nucleotides of SEQ ID NO:253. SD ¶ 17.

The '648 specification contains explicit written support for each of the nucleic acid molecules recited in the claims of each of groups I- and II. This support demonstrates that the inventors describe these nucleic acid molecules, thus satisfying the traditional test for written description articulated in *Vas-Cath*.

The Somerville Declaration, together with its underlying factual support, clearly demonstrates that the '648 specification would have conveyed to one of skill in the art that Appellants possessed the invention of claims 146-154 when the '648 specification was filed. The *Vas-Cath* test is satisfied.

b. *Lilly*

The factual record in this application also demonstrates that the '648 specification meets both of the tests for an adequate written description of a genus of nucleic acids set forth in *Lilly*. According to *Lilly*, adequate written description of a genus of nucleic acid molecules may be achieved by sufficiently describing a representative number of species within the genus either by defining their nucleotide sequence or by reciting "structural features common to the members of the genus, which features constitute a substantial portion of the genus." 119 F.3d at 1569, 43 U.S.P.Q.2d (BNA) at 1406. The description must permit one of skill in the art to "visualize or recognize members of the genus." 119 F.3d at 1559, 43 U.S.P.Q.2d (BNA) at 1406.

When read in conjunction with the '648 specification, it is Dr. Somerville's unequivocal opinion that, a Skilled Person would find that the '648 specification describes polynucleotides fully representative of the genus of polynucleotides of the Invention since:

a) the Skilled Person would recognize disclosure of SEQ ID NO:253 as fully representative of the genus of the Invention since it is a complete disclosure of the common structural feature (i.e., at least 50 contiguous nucleotides of SEQ ID NO:253) of the Inventions; and

b) the Skilled Person would recognize the vector containing a cDNA insert containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 and having flanking sequences, and would recognize that the vector is representative of a genus of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics. SD ¶ 18.

As discussed above, Dr. Somerville states that the specification provides an explicit description of the common structural feature of each of the claimed genera of nucleic acids, *i.e.*, the polynucleotide sequence of SEQ ID NO:253. SD ¶ 11. Dr. Somerville states that a description of polynucleotides containing at least *50* contiguous nucleotides of SEQ ID NO:253 is found on page 9, lines 6-10 of the '648 specification. SD ¶ 11. Dr. Somerville states that a Skilled Person, taking these disclosures together, would find specific description in the '648 application of the recited common structural feature for Group I claims: the sequence of at least 50 contiguous nucleotides of SEQ ID NO:253. SD ¶ 11.

Dr. Somerville states that the deposited vector that comprises the sequence set forth in SEQ ID NO:253 is fully representative of larger polynucleotides that can serve as probes or starting materials for probes. SD ¶ 18.

The '648 specification, therefore, clearly sets forth the structural feature of the claimed genera. The '648 specification also clearly describes a representative number of species within the species. Both of the tests set forth in *Lilly* are therefore satisfied.

Notably, based on the disclosure of the '648 specification, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within any one of the claims. SD ¶¶ 45, 20, 27, 31, 41.

c. *Enzo*

The factual record in this application also demonstrates that the '648 specification meets the tests for written description of nucleic acids articulated in *Enzo*. According to *Enzo*, "the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed." 296 F.3d at 1327, 63 U.S.P.Q.2d (BNA) at 1615. Again, the Somerville Declaration establishes that the '648 specification provides sufficient distinguishing information to permit one skilled in the art recognize the identity of the claimed subject matter.

The claims of Group I recite the distinguishing feature of at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253. Such is sufficient to describe the claimed invention so that the skilled artisan can recognize what is claimed.

The claim of Group II has the distinguishing feature of at least 50 contiguous nucleotides of an insert in a deposited vector. This feature is sufficient to describe the claimed invention so that the skilled artisan can recognize what is claimed. *Enzo* explicitly approved the use of a deposit to satisfy the written description requirement for a nucleic acid invention:

> we hold that reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited

material sufficient to comply with the written description requirement of § 112, ¶ 1."

Enzo, 296 F.3d at 1325, 63 U.S.P.Q.2d (BNA) at 1613.

The Somerville Declaration, together with its underlying factual support, clearly demonstrates that the '648 specification would have conveyed to one of skill in the art sufficient distinguishing information to permit one skilled in the art to visualize or recognize the identity of the claimed subject matter. The *Enzo* test is satisfied.

3. Specific assertions of the Examiner

The Examiner's arguments

The Examiner insists that the appealed claims are not sufficiently described to meet the requirements of 35 U.S.C. § 112, ¶1. This conclusion is based on a single assertion: since the claims are written in open form and, as a consequence, encompass a full length cDNA which is not described in the application, the claims are not adequately described by the specification. The following are exemplary statements by the Examiner during prosecution:

> 1. "However, claims 22-111 are directed to full length cDNA....." Paper no. 12, page 7, ¶ 7.
>
> 2. "The rejections under 35 USC 112, first paragraph is maintained because a full open reading frame is not described that is related to the claimed invention and therefore the claims (including newly filed claims 132-145) read on undescribed full open reading frames and their encoded polypeptides due to the presence of open language (consisting of) in all claims. Paper no 27 page 2.
>
> 3. "However the pending claims continue to read on an unknowable number of species of different polynucleotides that comprise different lengths of undescribed flanking sequences of the full-length cDNA to which SEQ ID NO:253 corresponds. Because newly filed claims 146-154 contain open language that reads on polynucleotides that comprise undescribed flanking sequences of the cDNA to which SEQ ID NO:253 corresponds the rejection for lack or written description has been maintained. Paper no. 32, text bridging pages 3 and 4

Appellants partially agree with the Examiner in the latter two assertions, and have acknowledged throughout prosecution that the claimed genera of polynucleotides encompass full length cDNA.[1] See, e.g., Amendment and Response filed November 1, 2002, page 8 and page 10. Appellants acknowledge that the '648 specification does not specifically describe the sequence of a full length cDNA (although the described sequences do have important utilities that the inventors recognized).

As explained in section I.D.1, *supra*, the claims do not require the claimed molecules be full length cDNA. As far as this record shows, no sequence of a polynucleotide containing more than 50 contiguous nucleotides of SEQ ID NO:253 or complement thereof, including the full-length cDNA, was in the art when Appellants filed the '648 specification. Thus, according to this record, nucleic acid molecules corresponding to the full-length cDNA and comprising more than 50 contiguous nucleotides of SEQ ID NO:253 or a complement thereof, are later-invented species of Appellants' generic invention.

The description of later-discovered species is not required to provide an adequate description of an earlier-discovered genus: "Our case law is clear that an applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention." *Rexnord Corporation v. Laitram Corporation*, 274 F.3d 1336, 1344, 60 U.S.P.Q.2d (BNA) 1851, 1856 (Fed. Cir. 2001). *See also In re Hogan and Banks*, 559 F.2d 595, 605-06, 194 U.S.P.Q. (BNA) 527, 537 (C.C.P.A. 1977); *United States Steel Corporation v. Phillips Petroleum Company*, 865 F.2d 1247, 1251-52, 9 U.S.P.Q.2d (BNA) 1461, 1465 (Fed. Cir. 1989). It is irrelevant whether a later-discovered subgenus consists of only one molecule or, as the Examiner alleges, "an unknowable number of species of different polynucleotides that comprise

[1] By "full-length" cDNA, the Office apparently means a cDNA that encodes a "complete open

different lengths of undescribed flanking sequences of the full-length cDNA to which SEQ ID NO:253 corresponds" Paper no 27, page 2. There is simply no basis in the law for the proposition that a genus which is adequately described in a specification as of the filing date nevertheless fails to meet the written description requirement because it is later shown to encompass even a large number of later-discovered species.

Nor is there any basis, either in the law or in this record, for assigning any particular importance to the later-discovered species of full length cDNA containing 50 contiguous nucleotides of SEQ ID NO:253 as part of assessing compliance with the written description requirement. The Examiner's first assertion -- "However, claims 22-111 are directed to full length cDNA....." Paper no. 12, ¶ 7. -- is not true. While the claims encompass a genus that includes the full-length cDNA, the claims are not so limited to this species. To say the claims are directed to full length cDNA is a baseless assertion that finds no support in the claims, the specification, or the record. In fact, the essential or critical element of Appellants' claims is 50 contiguous nucleotides of SEQ ID NO:253 or its complement. The Examiner has cited no basis in the law (nor are Appellants aware of any basis) for the proposition that a genus that is described in the specification fails to meet the written description requirement because one species, even a later-discovered, even preferred, species, is not disclosed. If the Examiner's rationale were correct, a claim to a chemical process limited to a disclosed temperature range of 0 to 100 degrees would not meet the written description requirement if there was an undisclosed later-discovered optimum temperature range of 50-60 degrees, which falls within that range. Such a conclusion would be contrary to decades of § 112 law.

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reading frame," which would encode a complete gene product.

In fact, the factual record of the present application establishes that the inventors specifically describes a wide variety of polynucleotide molecules containing at least 50 contiguous nucleotides of SEQ ID NO:253 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. SD ¶ 17. Neither the facts of this record nor the law provides the Examiner with a basis for viewing a later-discovered species, having a sequence that is not specifically recited in the claims, as a written description-defeating species of Appellants' earlier-invented genus.

Appellants have presented evidence to contradict the Examiner's assertions, have repeatedly questioned the support underlying the Examiner's rejection and have requested an Examiner's affidavit under 37 C.F.R. § 1.104(d)(2). See Response to October 21, 2001, Office Action filed November 1, 2002, page 7, first full paragraph. Under the case law and its own rules of practice, the Examiner is required to consider the factual evidence in the record, including the Somerville Declaration and its factual underpinnings, and either accept them as true or rebut them with a factual showing of its own. *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d (BNA) 1578, 1583 (Fed. Cir. 1996). In direct violation of this mandate, the Examiner has dismissed the evidence provided in the Somerville Declaration, including the supporting evidence provided as exhibits:

> Neither the applicants response nor the Declaration of Christopher R. Somerville provide reasons why such undescribed flanking sequences are in compliance with the written description requirements of 35 U.S.C. § 112, first paragraph. Paper no. 32 page 4.

The Examiner charges Dr. Somerville fails to provide reasons why flanking sequence are in compliance with the written description requirements of 35 U.S.C. § 112, ¶1.

However, in the same paragraph, the Examiner acknowledges vector polynucleotides that could be flanking sequences are well known to one of skill in the art:

> "The applicants arguments, and the arguments of the Declaration of Christopher R. Somerville focus on description of flanking vector sequences that might be linked to SEQ ID NO:253. It is conceded that the structure of such vector sequences are well known to one of skill in the art." Paper no. 32 page 4.

That said, the Appellants reason that since a large genus of vector flanking sequences are well known, and the sequence of SEQ ID NO:253 is provided in the '648 specification, a claim that recites a polynucleotide vector comprising 50 contiguous nucleotides of SEQ ID NO:253 should meet the written description requirements of 35 U.S.C. § 112, ¶1. However, claim 147, which recites a vector comprising 50 contiguous nucleotides of SEQ ID NO:253 or complement thereof, remains rejected.

Because the Examiner has refused Appellants' request for supporting evidence, the Board may not accept as fact any of the challenged statements of the Examiner. *Application of Lundberg*, 244 F.2d 543, 551, 113 U.S.P.Q. (BNA) 530, 537 (C.C.P.A. 1957). The factual record of this prosecution overwhelmingly establishes that the teachings of the '648 specification provide a sufficient written description of the subject matter of appealed claims 146-154.

The case law cited by the Examiner

The Examiner has cited *University of California v. Eli Lilly and Co*, *Fiers v. Sugano*, 984 F.2d 1164, 25 U.S.P.Q.2d (BNA) 1601 (Fed. Cir. 1993), *Amgen Inc. v. Chugai Pharmaceutical Co.* , 927 F.2d 1200, 18 U.S.P.Q.2d (BNA) 1016 (Fed. Cir. 1991), *Fiddes v. Baird* 30 U.S.P.Q.2d 1481 (Bd. of Appeals 1993) in support of the written description rejection of the appealed claims. None of this case law supports the rejection of the appealed claims.

Before each of these cases is addressed in turn, the Appellants note that the disputed patents in the above cases were filed between the late 1970s and the mid-1980s. The field of recombinant DNA technology is rapidly evolving, and most major technological advances have been made in the last 20 years. SP ¶ 47. A Skilled Person had a dramatically higher skill level in March 2000 as compared to the filing dates disputed in the above cases. *Id.* Dr. Somerville does not believe that a statement regarding what one of ordinary skill can or cannot do in the above cases could be used as evidence with respect to what the Skilled Person in March of 2000 could or could not do. *Id.* As such, each of the above cases can not be used to support these rejections for two reasons. Firstly, the cases are simply misapplied. Secondly, the decisions in these cases turn on what one of skill in the art could or could not do at the time of filing approximately 20 years ago, which, as we have established, is dramatically different to what one of skill in the art could or could not do in March 2000.

Lilly

The Examiner misapplies *Lilly*. The patents at issue in *Lilly* claimed recombinant plasmids containing a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin. The patent specification, however, disclosed a cDNA sequence only for rat insulin, but not for the human or any other vertebrate. The only defining feature recited in the claims of *Lilly* was that the sequence encoded insulin. The Federal Circuit found that recitation of a function of the sequence was not adequate; rather, the specification must provide a structure. Specifically the court stated:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can

> do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Lilly, 119 F.3d at 1568, 43 U.S.P.Q.2d (BNA) at 1406 (citations omitted).

The Federal Circuit concluded that only those claims limited to the rat cDNA were valid, and found the generic claim and claims directed to the human insulin-encoding cDNA were invalid as not being adequately described under 35 U.S.C. §112, ¶1. 119 F.3d at 1562-63, 43 U.S.P.Q.2d (BNA) at 1401. of the members of the genus." 119 F.3d at 1568, 43 U.S.P.Q.2d (BNA) at 1406.

Appealed claims 146-154 differ notably from those at issue in *Lilly* in that each appealed claim particularly recites a specific nucleotide sequence. Only molecules containing such a sequence are literally embraced by the claims, and molecules not containing such a sequence are not. The skilled worker can easily make this determination. SD ¶ 45. In direct contrast, claims of U.S. Patent 4,625,525 at issue in *Lilly* did not recite any particular sequence and merely recited, for example, "a subsequence having the structure of the reverse transcript of an mRNA . . . which mRNA encodes insulin." *Lilly*, 119 F.3d at 1563, 43 U.S.P.Q.2d (BNA) at 1401. Thus, in contrast to the claims at issue in *Lilly*, the appealed claims do not rely solely upon a function of the claimed polynucleotides, but rather recite structural characteristics, *i.e.*, at least 50 contiguous nucleotides selected from SEQ ID NO:253 or complement thereof (Group I claims) or at least 50 contiguous nucleotides of either strand of nucleotide sequence of an inserted contained in a deposited vector (Group II claim).

Each of claims 146-154 is structurally limited and specifies a particular polynucleotide sequence that a nucleic acid molecule must encode to fall within the scope of the claim. The '648

specification discloses those precise sequences and provides an extensive description of additional nucleic acid molecules comprising those sequences. SD ¶¶ 11, 13-17. Those skilled in the art quite easily "visualize or recognize" whether or not any particular nucleic acid molecule encodes the required amino acid sequence and can quite easily determine whether that nucleic acid molecule is encompassed within a particular claim. Somerville Declaration I, ¶ 29. None of the claims contains any limitation that creates any difficulty in identifying whether a nucleic acid molecule is a member of the genus. Accordingly, *Lilly* supports the patentability of the pending claims. The claims satisfy the written description test as set out in *Lilly*.

Fiers

Similarly, the Examiner misapplies *Fiers*. *Fiers* reports an award of priority to Sugano in a three-way interference proceeding between Revel, Sugano, and Fiers. 984 F.2d at 1166, 25 U.S.P.Q.2d (BNA) at 1602. In this case, the Federal Circuit applied the holding in *Amgen* to an interference case where three parties (Fiers, Revel, and Sugano) claimed patent rights to the DNA encoding human fibroblast beta interferon (IFN-β). Fiers asserted priority based on his conception of a method for isolating the IFN-β DNA in 1979 or early 1980, coupled with due diligence towards a constructive reduction to practice on April 3, 1980. *Id* Before he isolated the DNA, Fiers had disclosed his method to two American scientists, both of whom submitted affidavits that Fiers' method would have allowed a person of ordinary skill in the art to isolate the IFN-β DNA sequence without undue experimentation. *Id.*

Fiers asserted that the stringent written description requirement set forth in *Amgen* only applied when the disclosed method for isolating a DNA sequence could not easily be carried out by one of ordinary skill in the art. *Id.* at 1169. Fiers also argued that *Amgen* allows conception of a DNA sequence by its method of isolation. *Id.* The Federal Circuit rejected both of these

arguments, stating that Fiers was focusing inappropriately on the issue of enablement rather than written description. *Id.* The court also stated that, before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, cannot constitute more than conception of the substance claimed as a process (product-by-process claim). *Id.* Conception of a substance claimed *per se*, without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties. *Id.*

The appealed claims recite a structural definition of the claimed Invention -- at least 50 contiguous nucleotides selected from SEQ ID NO:253 or complement thereof (Group I claims) or at least 50 contiguous nucleotides of either strand of nucleotide sequence of an inserted contained in a deposited vector (Group II claim). Further, the specification provides an extensive description of larger molecules comprising those sequences. SD ¶¶ 11, 13-17. The '648 application therefore meets the standard set out in *Fiers*. *Fiers*, therefore, cannot be used to assert that the subject matter of the appealed claims are not adequately described in the '648 specification. Instead, since the '648 application meets the conception test provided by Fiers, Fiers may be used in *support* of an assertion that the subject matter of the appealed claims are adequately described in the '648 specification.

Fiddes v. Baird

In making the rejection, the Examiner also relied on the 1993 decision in *Fiddes v. Baird*, 30 U.S.P.Q.2d 1481 (Bd. App. Pat. Inf. 1993) in which the Board cited *Fiers* in a priority contest over inventorship of recombinant DNA molecules encoding fibroblast growth factors ("FGFs"). Baird claimed priority on the basis of an application that set forth the amino acid sequence for bovine pituitary FGF and a *theoretical* DNA sequence encoding that protein, along with a

method for obtaining a cDNA corresponding to the protein. The application did not teach the actual naturally-occurring DNA sequence encoding the FGF protein. *Id.* at 1482-81. Since the actual nucleotide sequence of the naturally-occurring DNA molecule was not disclosed, the Board followed *Fiers* in determining that Baird was not in possession of the broad class of naturally-occurring genes encoding mammalian FGFs:

> An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.
>
> * * *
>
> If a conception of a DNA requires a specific definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity....[O]ne cannot describe what one has not conceived. *Id.* at 1482-83, *citing Fiers,* 984 F.2d at 1170-71.

In contrast, the appealed claims are not directed to theoretical molecules that the Appellants hope to be able to obtain by a disclosed method. The appealed claims are directed to molecules comprising specific sequences that Appellants actually obtained. The '648 specification discloses those precise sequences and provides an extensive description of additional nucleic acid molecules comprising those sequences. SD ¶¶ 11, 13-17. *Fiddes v. Baird,* therefore, cannot be used to assert that the subject matter of the appealed claims are not adequately described in the '648 specification. Instead, since the '648 application meets the conception test provided by *Fiddes v. Baird*, *Fiddes v. Baird* may be used in *support* of an assertion that the subject matter of the appealed claims are adequately described in the '648 specification.

Amgen, Inc. v. Chugai Pharmaceutical, Co.

In *Amgen, Inc. v. Chugai Pharmaceutical,* 927 F.2d 1200, 18 U.S.P.Q.2d (BNA) 1016 (Fed. Cir. 1991), *Co.*, the Federal Circuit considered an Amgen patent issued on October 27, 1987, which contained claims to the DNA sequence encoding human erythropoietin (EPO). Amgen claimed priority of invention based on isolation of EPO clones in 1983.

Prior to Amgen's cloning of the EPO gene, however, Genetics Institute ("GI") had isolated and purified the EPO protein, and had also disclosed a strategy for obtaining the EPO DNA sequence. *Id.* at 1205. The USPTO issued a patent to GI on June 30, 1987 with claims to the EPO protein itself. *Id.* at 1203. GI did not actually clone the EPO cDNA until August 1984, and began making recombinant EPO using the cDNA shortly thereafter. *Id.* at 1205-06.

The Federal Circuit held that the Amgen patent was not invalidated by GI's earlier-disclosed isolation strategy to obtain the EPO DNA and its sequence, even though this strategy eventually resulted in the actual cloning of the gene by GI. *Id.* at 1206. GI's disclosure of the protein, and a method for isolating and purifying the EPO DNA sequence, was insufficient to constitute actual conception of the DNA encoding EPO. *Id.* Applying chemical case law precedent,[2] the Amgen court stated:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principle biological property, *e.g.,* encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any

[2] See *Oka v. Youssefyeh,* 849 F.2d 581, 583 (Fed. Cir. 1988). The court, in Amgen, classified DNA as a complex chemical compound and held that "it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and ... describe how to obtain it." *Amgen,* 927 F.2d at 1206.

material with that biological property. *Amgen v. Chugai Pharmaceuticals,* 927 F.2d at 1206 (citations omitted)

Thus, since GI had not yet cloned the DNA sequence encoding EPO when it filed its patent application, and the specification only suggested a possible method by which to isolate the DNA sequence, GI could not have a mental conception of the EPO DNA sequence at the time the application was filed. *Id.* The court did not invoke the requirement that the actual DNA sequence be disclosed, but only that the DNA be defined in a way to distinguish it from other chemicals along with a description of how to obtain it. *Id.*

In contrast, the appealed claims are not directed to theoretical molecules that the Appellants hope to be able to obtain by a disclosed method. The appealed claims are directed to molecules comprising specific sequences that Appellants actually obtained. The '648 specification discloses those precise sequences and provides an extensive description of additional nucleic acid molecules comprising those sequences. SD ¶¶ 11, 13-17. *Amgen*, therefore, cannot be properly applied to assert that the subject matter of the appealed claims are not adequately described in the '648 specification. Instead, since the appealed claims recite a structure that that is fully described in the '648 specification SD ¶¶ 11, 13-17, the application actually passes the tests provided by *Amgen.*

The Facts of the Cited Cases are Distinct from those of the Instant Application

None of the cases cited in support of the written description rejection of claims 146-154 provide a situation analogous to the one at hand. In each of the cited cases, a party was attempting to broadly claim a DNA sequence based on its function (e.g., as in *Lilly*, which relied upon the function of the cDNA in encoding insulin) or where no sequence is described, but rather only a method for obtaining it (*e.g.*, as in *Fiers* and *Fiddes*).

None of the cited cases consider a situation where the specification described a sequence present in all members of the claimed genus of sequences, or other structural characteristic common to all members of the claimed genus. Further, without such a common structural characteristic, the court found in each case that the specification did not describe the claimed polynucleotides "so as to distinguish it from other materials." In contrast, the appealed claims do provide such a common structural feature. As such, the facts of the cited cases are not analogous to those of the instant case; in fact, the reasoning set out in the cited cases actually support a finding that the appealed claims are adequately described by the instant application.

As stated in *Amgen*, DNA is simply a chemical compound that can be conceived of by a mental picture of the structure of the compound or whatever characteristics sufficiently distinguish it. In *Lilly*, the court stated that in claims involving chemical materials, generic formulae must indicate with specificity what the claims encompass such that one skilled in the art can distinguish the formula from other formulas and can identify many of the species the claims encompass. Such a formula generally constitutes an adequate written description of the claimed genus. *Lilly* also held that a description of a genus of cDNAs may be achieved by recitation of structural features common to the members of the genus. Moreover, the court in *Fiers* held that conception of a substance requires conception of its structure, formula, or definitive chemical or physical properties.

In the instant application, the claims recite an element – either a particular nucleotide sequence or an insert of a deposited vector -- that provides a distinguishing feature common to the genus of claimed polynucleotides. The recited element provides a structural feature common to all the members of the claimed genera, serves to define the claimed genus. With the knowledge of the nucleotide sequence of SEQ ID NO: 253 and with the availability of the insert

of the deposited vector, one skilled in the art can easily determine if a sequence is a member of the claimed genus.

Each of the appealed claims recite a critical defining feature – one that was said to be lacking in the claims considered and rejected in each of *Amgen, Fiers, Lilly,* and *Fiddes*. The feature of the claims defines the claimed polynucleotide "so as to distinguish it from other materials." *Amgen vs. Chugai*, 927 F.2d at 1206. The recited sequence also provides "a structural or equivalent definition" of the claimed polynucleotide. *Fiers*, 984 F.2d at 1169. *See also Fiddes*, 30 U.S.P.Q.2d at 1482-83. Moreover, the sequence recited in the claims provides "a recitation of structural features common to the members of the [claimed] genus." *Lilly*, 119 F.3d at 1568-69. Thus, it is much more than a mere wish to obtain a composition – it defines the composition.

4. Appellants' use of the term "comprising" is entirely proper

In contrast to the Examiner's position, the present application presents a strong case for issuing open-ended claims.

The appealed claims are based on the inventors' discovery of polynucleotides, which are defined in the claims as containing at least 50 contiguous nucleotides selected from SEQ ID NO:253 or having at least 50 contiguous nucleotides of either strand of a nucleotide sequence of an insert contained in a deposited vector. The claimed polynucleotides may be used to detect polynucleotides that are expressed at higher levels in cancerous cells as compared to non-cancerous cells. The sequence of SEQ ID NO:253 is provided in the '648 specification, and provides an extensive description of additional nucleic acid molecules comprising those sequences. SD ¶¶ 11, 13-17. The claimed polynucleotides may serve as probes or starting materials for probes in cancer diagnostics. SD ¶ 18. There is no criticality to sequences flanking the claimed polynucleotides. SD ¶ 17, Rather, selection of such flanking sequences is an

arbitrary matter of design. *Id.* The Skilled Person would readily appreciate from the specification that the sequence of SEQ ID NO:253 can be incorporated within a vast number of larger polynucleotides, and that each of these sequences is identifiable as having at least 50 contiguous nucleotides of SEQ ID NO:253. *Id.*

The present application, therefore, is simply not a case in which Appellants are attempting to claim DNA fragments in open language without knowing the identity or function of the gene to which the fragments belong, or where the fragments have no demonstrated or medically important utility. Any polynucleotide containing 50 contiguous nucleotides of SEQ ID NO:253, no matter how large the polynucleotide, has a utility as a diagnostic probe for cancer, or a starting material for such a probe. SD ¶ 18.

The U.S. Patent and Trademark Office routinely issues patents that claim DNA molecules encoding full-length genes using open language, as indicated by numerous issued patents. The Office should not find anything per se objectionable about open-ended nucleic acid claims, regardless of whether the claim-recited nucleic acid is a fragment of a so-called "full-length" cDNA. There is no reasonable basis under the guise of the written description requirement or any other portion of the patent laws for allowing open-ended claims if the recited sequence is "full-length" while denying open-ended claims solely because the claims are defined by a recited sequence that is only a portion of a "full-length" cDNA. To the extent the Office has applied this distinction in this case, it is an arbitrary distinction unfounded in the law, and it should be disregarded.

There is good reason for allowing open-ended claims to useful polynucleotide molecules like those invented by Appellants. In the recombinant nucleic acid field, making and using specific polynucleotide molecules routinely involves incorporating the specific polynucleotides

into larger molecules, including cloning and expression vectors. Specific polynucleotide molecules retain their essential utility when linked to additional sequences. Obviously, the variety of useful larger molecules comprising a specific polynucleotide sequence is essentially limitless. In the recombinant DNA field, the practical reality is that larger polynucleotide molecules into which the inventive polynucleotide molecule can be inserted should be viewed simply as the functional milieu in which an inventive sequence can be made and used. In this context, inventors of polynucleotides would be deprived of meaningful patent protection if claims were limited by closed language to the inventive polynucleotide or to specific larger molecules into which Appellants actually incorporated the inventive polynucleotide molecule. Others could use the inventions but avoid the claims easily merely by using the inventive sequences in unclaimed larger molecules. Closed claims for nucleic acids would utterly eviscerate patent protection for those inventions.

These concerns apply unequivocally to Appellants' claims. The closed claims offered by the Examiner would not provide Appellants with patent protection commensurate with their invention. The record shows that Appellants specifically teach, and the skilled worker was well aware, that the inventive sequences should be incorporated into larger molecules to make and use them. The record shows that closed claims would deprive Appellants of patent protection on polynucleotides that are fully described in the specification, a representative example of which is deposited at the A.T.C.C. See Somerville Declaration at ¶¶ 11-18. A polynucleotide containing an addition of a few nucleotide bases or even a single nucleotide base to the end of the recited polynucleotide sequence would retain the utility of the disclosed molecules and yet be outside of the scope of such closed-ended claims. In short, denying Appellants the open-ended claims

would permit anyone to avoid Appellants' claims while taking full advantage of Appellants' contribution to the art.

The U.S. patent system was not designed to provide such meaningless protection, and the Office does not achieve the constitutional purpose of the patent system when it attempts to force patentees to accept claims of literally no value. As the Court of Customs and Patent Appeals has stated:

> The public purpose on which the patent law rests requires the granting of claims commensurate in scope with the invention disclosed. This requires as much the granting of broad claims on broad inventions as it does the granting of more specific claims on more specific inventions. It is neither contemplated by the public purpose of the patent laws nor required by the statute that an inventor shall be forced to accept claims narrower than his invention in order to secure allowance of his patent. It is, however, consistent with this public purpose embodied in the pertinent statutory requirement that the *invention claimed* shall be no broader than the *invention set forth* in the written description forming part of the specification.

In re Sus and Schaefer, 306 F.2d 494, 497, 134 U.S.P.Q. (BNA) 301, 304 (C.C.P.A., 1962), emphasis in original.

Open claims to inventive nucleic acid sequences are analogous to open claims in other fields. For example, claims are routinely allowed that encompass all pharmaceutical formulations of an inventive pharmaceutical without any limitation on the type of pharmaceutical formulation. Where the invention is in the agent, there is no justification for restricting the type of formulation in which the agent could be included, even though such claims would read on future discovered formulations that contain the agent and even where all possible formulations are not described in the application

The clear rationale for permitting applicants to claim pharmaceutical formulations comprising patentable agents using open-ended language is that requiring any claim limitation on

a collateral feature (such as the specific formulation) would allow competitors to use the invention simply by altering a nonessential collateral feature. The law does not limit the inventor of a new pharmaceutical agent to claims covering only the agent itself or the specific formulations the inventor actually made.

In other words, there is no way for Appellants to obtain claims commensurate with Appellants' invention of new and useful sequences other than to claim nucleic acid molecules comprising those sequences. Closed claims like those that would likely satisfy the Examiner (e.g., directed to a "polynucleotide consisting of at least 50 contiguous nucleotides of SEQ ID NO:253") would be no more useful or fair than a claim to "a device consisting of [an inventive valve]" that could not be enforced against a manufacturer or user of a larger device comprising the valve or a claim to a "new pharmaceutical agent" that could not be enforced against a manufacturer who incorporated the agent into a formulation for administration.[3]

The Examiner has relied on its core objection that the appealed claims encompass molecules that are larger than at least 50 contiguous polynucleotides of SEQ ID NO:253 that could include full length cDNA, and that the sequence of this full length cDNA is not specifically described in the specification. In other words, the Examiner is reading a limitation in

[3] Not only does the law provide no justification for imposing unique patentability requirements on inventions of useful nucleic acid sequences, the law actually proscribes any such differential treatment. Article 27.1 of the TRIPS Agreement states in part that "patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced." Agreement on Trade-Related Aspects of Intellectual Property Rights, April 15, 1994, Marrakech Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments – Results of the Uruguay Round, 33 I.L.M. 81 (1994). If the United States, through TRIPS, forces the rest of the world to comply with western-style intellectual property norms, we ourselves should not treat any particular technology differently than all other technologies. The uniquely heightened written description standard that the U.S. Patent and Trademark Office seems to be applying to nucleic acid inventions in this case would violate this portion of Article 27.1.

to the claim which is simply not present: the sequence of the full length cDNA corresponding to SEQ ID NO:253.

The sequence of the full length cDNA corresponding to SEQ ID NO:253 is not taught in the '648 application, is not specifically recited in the claims and, as a point of fact, would represent later-discovered species within those claims. These later-discovered species may have new uses not possessed by all molecules claimed by Appellants, and in fact they may be patentable over Appellants' claims. But no case has ever held that the later development of a separately patentable species renders a prior genus unpatentable. No case has ever questioned that later-invented species may be dominated by earlier generic inventions -- in fact that situation is commonly the case and is understood in the law to be normal in fast-evolving arts. There is no uniquely-applicable basis in law or science for deeming generic nucleic acid sequence patents meeting the statutory requirements of patentability inappropriate simply because they dominate any later-discovered full length genes. Such a special, hindsight-based evaluation of generic nucleic acid claims would not only be contrary to fundamental principles of patent law, but in the long run would surely undermine the nucleic acid art. Thus, the Examiner's objection is baseless, does not respond to the legal or policy issues raised by Appellants, and should be disregarded.

E. Conclusion

Appellants have provided the U.S. Patent and Trademark Office with an extensive factual record which establishes without question that all the claims of groups I and II (claims 146-154), each of which should be separately analyzed, meet the written description requirement of 35 U.S.C. § 112, ¶1. There is no evidence in the record to the contrary. The evidentiary record establishes that the '648 specification conveys to one of skill in the art that Appellants possessed

the invention to which the appealed claims are directed when that specification was filed. *Vas-Cath*, 935 F.2d at 1563-64, 19 U.S.P.Q.2d (BNA) at 1117. The evidentiary record establishes that the '648 specification describes the claimed invention so that one skilled in the art can recognize what is claimed. *Enzo*, 296 F.3d at 1327, 63 U.S.P.Q.2d (BNA) at 1615. The evidentiary record establishes that the '648 specification sufficiently described a representative number of species within each recited genus of polynucleotide molecules to permit one of skill in the art to "visualize or recognize members of the genus." *Lilly*, 119 F.3d at 1559, 43 U.S.P.Q.2d (BNA) at 1406.

In making the written description rejection, the Examiner has ignored the full extent of the evidentiary record and has improperly focused on unrecited features defining species of full length cDNA. The sequence of the full-length cDNA is not specifically recited in the claims or essential to Appellants' invention. It would be a later-discovered species of the generic invention embraced by appealed claims 146-154. The '648 specification need not have described them.

The rejection should be reversed.

REQUEST FOR ORAL HEARING

Appellants request an oral hearing on this appeal, and enclose two additional copies of this Brief in connection therewith.

CONCLUSION

For the reasons given above, the rejection of claims 146-154 under 35 U.S.C. § 112, ¶1 is improper. The Board of Patent Appeals and Interferences should reverse the rejection.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

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Date: March 5, 2004

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APPENDIX 1. APPEALED CLAIMS

146. An isolated polynucleotide comprising at least 50 contiguous nucleotides of a sequence selected from SEQ ID NO:253 and the complement thereof.

147. A vector comprising a polynucleotide of claim 146.

148. A host cell comprising the vector of claim 147.

149. An isolated polynucleotide comprising at least 50 contiguous nucleotides of SEQ ID NO:253 and which hybridizes under stringent conditions to a polynucleotide of a sequence selected from SEQ ID NO:253 and the complement thereof.

150. The polynucleotide of claim 149, wherein hybridization is conducted at least 50°C and using 0.1XSSC (9 mM saline/0.9 mM sodium citrate).

151. A polynucleotide comprising at least 50 contiguous nucleotides of either strand of a nucleotide sequence of an insert contained in a vector deposited as clone number M00001448D:C09 of A.T.C.C. Deposit Number 207068, wherein the insert is a human cDNA and the clone is obtained from a human cDNA library.

152. An isolated polynucleotide comprising at least 50 contiguous nucleotides of SEQ ID NO:253, said polynucleotide obtained by amplifying a fragment of cDNA using at

least one polynucleotide primer comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of: SEQ ID NO: 253 and the complement thereof.

153. A vector comprising a polynucleotide of claim 152.

154. A host cell comprising the vector of claim 153.

COPY

Copy OF DECLARATION OF CHRISTOPHER SOMERVILLE UNDER 37 C.F.R. § 1.132	Attorney Docket	2300-1481
	First Named Inventor	Williams et al.
	Application Number	09/297,648
	Filing Date	March 10, 2000
	Group Art Unit	1631
	Examiner Name	J. Brusca
	Title: *Human Genes and Gene Expression Products II*	

Dear Sir:

1. I, Christopher R. Somerville, declare and say I am a resident of the State of California. My residence address is 5 Valley Oak, Portola Valley, CA 94028.

2. I hold a B.Sc. degree in Mathematics, which I received from the University of Alberta, Canada in 1974. I further hold M.Sc. and Ph.D. degrees in Genetics, which I received from the University of Alberta, Canada in 1976 and 1978, respectively.

3. I am a Director of the Carnegie Institution of Washington Department of Plant Biology and a Professor of the Department of Biological Sciences at Stanford University. I am an elected member of the U.S. National Academy of Sciences, and an elected fellow of the Royal Societies of London and Canada. I serve on the editorial boards of several international peer-reviewed journals and have served on several panels for the NIH, NSF and USDA. I have worked in the field of recombinant DNA technology for over 20 years and have published over 150 articles in the fields of genetics, biochemistry, molecular biology and genomics (see curriculum vitae attached).

4. I have reviewed U.S. Patent Application No. 09/297,648 (hereinafter the '648 application), the first Office Action (specifically section No. 7) mailed November 29,

2000, the final Office Action (specifically section No. 12) mailed October 2, 2001, and the Advisory Action mailed May 31, 2002 in the '648 application.

5. I understand the inventions at issue (hereinafter "Inventions") are defined by the following claims:

Claims 146-148

Claim 146 is a formula in which the Invention is defined as a genus of polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 50 contiguous nucleotides of SEQ ID NO:253. I understand that the genus of polynucleotides defined by Claim 146 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than the specified contiguous region. Claim 147 defines the Invention as a vector containing the Invention of Claim 146, and Claim 148 defines the Invention as host cells containing the Invention of Claim 147.

Claims 149-150

Claim 149 is a formula in which the Invention is defined as a genus of polynucleotides characterized by the common structural feature of (1) a length that is a minimum of 50; and (2) sufficiently structural similarity to SEQ ID NO:253 to allow the polynucleotide to hybridize under stringent conditions to a polynucleotide having a sequence of SEQ ID NO:253. Claim 150 further defines the stringent conditions used for hybridization.

Claim 151

Claim 151 defines the Invention as a genus of polynucleotides characterized as containing a sequence that is the same as the sequence of an cDNA insert found in the clone number M00001448D:C09, deposited with the ATCC. I understand that the genus of polynucleotides defined by claim 151 includes polynucleotides that contain additional sequences (i.e. flanking sequences) other than that specified by SEQ ID NO:253.

Claims 152-154

Claim 152 defines the Invention as a genus of isolated polynucleotides characterized as having the common structural feature of a nucleotide sequence containing a minimum of 50 contiguous nucleotides of SEQ ID NO:253, obtained as a product of amplification using at least one oligonucleotide primer that contains at least 15 contiguous nucleotides of the sequence of SEQ ID NO:253. Claim 153 defines the Invention as a vector containing the Invention of Claim 152, and Claim 154 defines the Invention as host cells containing the Invention of Claim 153.

In this Declaration, I will be addressing these Inventions.

6. I have been asked to opine of the following questions:

a) Would one of ordinary skill in the art to which the Inventions pertain (hereinafter the "Skilled Person") would conclude from a review of the '648 application as a whole that the Inventions are described therein and the inventors were in possession of the Inventions?

b) Would the Skilled Person conclude from a review of the '648 application as a whole that the disclosures therein are representative of the genera defined by the Inventions?

It is my opinion, based on the facts and reasoning set forth below, that the answer to each of these questions is "yes."

Skilled Person

7. It is my understanding that the application is to be viewed from the standpoint of one of ordinary skill in the art in the relevant field at the time of filing of the application (referred to here as the "Skilled Person"). The '648 application was filed on March 10, 2000 and relates to the field of recombinant DNA technology. I would expect a Skilled Person in the field of recombinant DNA technology in March 2000 to

have been represented by a scientist with a Ph.D. degree and two years of post-doctoral training. I consider that such a Skilled Person would have the ability to analyze a DNA sequence using the common general knowledge, tools, and methods available in the field and without inventive effort. Furthermore, such a Skilled Person would have had access to and would have used as needed persons of ordinary skill in other technical fields, such as (by way of illustration and not limitation) cellular biology, oncology, biochemistry, immunology, physiology and diagnostics.

8. In March 2000, the common general knowledge, tools, and well-known methods available in this field were extensive. Widely available methods included nucleotide hybridization, nucleic acid cloning, polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR), gene sequencing and cDNA library construction and screening. In addition, several "bioinformatics" tools were available, such as bioinformatics programs for searching a database of nucleic acids sequences for similar nucleic acid sequences (e.g. BLAST), programs for comparing two nucleic acid sequence (e.g. the BESTFIT or GAP programs as provided by the University of Wisconsin's GCG program) and programs for predicting and annotating coding sequences of genes (e.g. GENSCAN and XGRAIL).

9. Since I a) regularly attended external and internal meetings on molecular biology topics at which Skilled Persons presented their research, b) regularly read and reviewed scientific literature in which Skilled Persons presented their research, and c) was head of a laboratory in which several Skilled Persons have received training, prior to and during March 2000, I believe that I am qualified by training and experience to address what a Skilled Person would have understood from a reading of the specification of U.S. Patent Application No. 09/297,648 as of its filing date on March 10, 2000.

10. The following remarks constitute the basis for my opinion that the Skilled Person would conclude, from a review of the '648 application as a whole, that the Inventions were described in the '648 application and in the inventors' possession, and further that the disclosure of '648 application contains representative examples of the Inventions.

Claims 146-148

11. The specification describes the Inventions of Claims 146-148 in a number of passages, including the following:

In the sequence listing submitted as part of the application, SEQ ID NO:253 is provided as follows:

<400> 253
gaacaaagaa ggaatgtctt cctcatgttt gggtctatag aagacgttaa agaaaacttc 60
aagaaagtgg gtttgaggca tgagccacca cgcctggcca aaggatttaa tgaattaatg 120
gatgtacagt gctggggctg ttattctagg gcctgcattg agactcacat tttgccatca 180
aaagcctttt aagaggtgga ggttgcggtg agctgacatg gtgccactgc actccggcct 240
gagtgacaga gtgagactct gtctcacaaa aaaaataatg ccctttaaat aatgaataat 300

An actual clone encompassing the sequence of SEQ ID NO:253 was deposited with the A.T.C.C. as clone number M00001448D:C09 of ATCC Deposit Number 207068.

On page 9, lines 6- 10 of the specification, particular lengths of regions of SEQ ID NO:253 are described:

> Isolated polynucleotides and polynucleotide fragments of the invention comprise at least about 10, about 15, about 20, about 35, about 50, about 100, about 150 to about 200, about 250 to about 300, or about 350 contiguous nucleotides selected from the polynucleotide sequences as shown in "SEQ ID NOS:1-5252."

Taking these disclosures together, the Skilled Person would find described in the '648 application all sequences of at least 50 contiguous polynucleotides contained within SEQ ID NO:253.

12. I am informed that in the language of patent law the term "comprise" as used in the above claims means that flanking sequences can be present in addition to the specified sequence. A genus of polynucleotides containing flanking regions is describe in the '648 application, as discussed further below.

13. Nucleic acid probes containing the specified sequence, which a Skilled Person would recognize as often longer than the specified sequence from the SEQ ID, are described in several positions in the specification, for example:

on page 9, lines 15-22:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in "SEQ ID NOS:1-5252." The probes are preferably at least about 12, 15, 16, 18, 20, 22, 24, or 25 nucleotide fragment of a corresponding contiguous sequence of "SEQ ID NOS:1-5252", and can be less than 2, 1, 0.5, 0.1, or 0.05 kb in length. The probes can be synthesized chemically or can be generated from longer polynucleotides using restriction enzymes. The probes can be labeled, for example, with a radioactive, biotinylated, or fluorescent tag. Preferably, probes are designed based upon an identifying sequence of a polynucleotide of one of "SEQ ID NOS:1-5252."

and on page 10, lines 12-19:

> The subject nucleic acid compositions can be used to, for example, produce polypeptides, as probes for the detection of mRNA of the invention in biological samples (*e.g.*, extracts of human cells) to generate additional copies of the polynucleotides, to generate ribozymes or antisense oligonucleotides, and as single stranded DNA probes or as triple-strand forming oligonucleotides. The probes described herein can be used to, for example, determine the presence or absence of the polynucleotide sequences as shown in "SEQ ID

> NOS:1-5252" or variants thereof in a sample. These and other uses are described in more detail below.

Furthermore, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY., which is incorporated by reference into the application, discloses several types of probes that contain flanking sequences, including hybridization probes, oligonucleotide probes, RNA probes, plasmid probes and polymerase chain reaction probes. For example, a Skilled Person would recognize that a probe may contain polylinker sequences, or an oligonucleotide "tail". The Skilled Person would also know that much longer sequences, such as vectors containing the sequence specified from the SEQ ID can be used as probes.

14. Vectors containing the specified sequence, which a Skilled Person would recognize as always being longer than the specified sequence, are described in several positions in the specification. For example, on page 10, lines 3-6, that an Invention can be contained in a vector is recited:

> The polynucleotides of the invention can be provided as a linear molecule or within a circular molecule. They can be provided within autonomously replicating molecules (vectors) or within molecules without replication sequences. They can be regulated by their own or by other regulatory sequences, as is known in the art.

On page 15, lines 5-12, several types of vector, including expression vectors, viral vectors, non-viral vectors and plasmids are described:

> Appropriate polynucleotide constructs are purified using standard recombinant DNA techniques as described in, for example, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY, and under current regulations described in United States Dept. of HHS, National Institute of Health (NIH) Guidelines for Recombinant DNA Research. The gene product encoded by a polynucleotide of the invention is

> expressed in any expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems. Suitable vectors and host cells are described in U.S. Patent No. 5,654,173.

And on page 16, lines 16-23, several more vectors are described:

> Polynucleotide molecules comprising a polynucleotide sequence provided herein propagated by placing the molecule in a vector. Viral and non-viral vectors are used, including plasmids. The choice of plasmid will depend on the type of cell in which propagation is desired and the purpose of propagation. Certain vectors are useful for amplifying and making large amounts of the desired DNA sequence. Other vectors are suitable for expression in cells in culture. Still other vectors are suitable for transfer and expression in cells in a whole animal or person. The choice of appropriate vector is well within the skill of the art. Many such vectors are available commercially.

And numerous examples of types of retroviral vectors, alphaviral vectors, adeno-associated viral vectors and adenoviral vectors are described in the specification on page 74, line 13 to page 75, line 19.

15. On page 8 lines 16-21 of the specification, cDNA polynucleotides containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, are described:

> The term "cDNA" as used herein is intended to include all nucleic acids that share the arrangement of sequence elements found in native mature mRNA species, where sequence elements are exons and 3' and 5' non-coding regions. Normally mRNA species have contiguous exons, with the intervening introns, when present, being removed by nuclear RNA splicing, to create a continuous open reading frame encoding a polypeptide of the invention..

Furthermore, the actual vector encompassing the sequence of SEQ ID NO:253 was deposited with the A.T.C.C. is a cDNA clone.

16. Finally, on page 8, line 13 to page 9 line 2, the specification discloses a gene containing the specified sequence, which a Skilled Person would recognize as longer than the specified sequence, is described:

> The subject nucleic acids can be cDNAs or genomic DNAs, as well as fragments thereof, particularly fragments that encode a biologically active gene product .....
>
> A genomic sequence of interest comprises the nucleic acid present between the initiation codon and the stop codon, as defined in the listed sequences, including all of the introns that are normally present in a native chromosome. It can further include the 3' and 5' untranslated regions found in the mature mRNA. It can further include specific transcriptional and translational regulatory sequences, such as promoters, enhancers, *etc.*, including about 1 kb, but possibly more, of flanking genomic DNA at either the 5' and 3' end of the transcribed region. The genomic DNA can be isolated as a fragment of 100 kbp or smaller; and substantially free of flanking chromosomal sequence. The genomic DNA flanking the coding region, either 3' and 5', or internal regulatory sequences as sometimes found in introns, contains sequences required for proper tissue, stage-specific, or disease-state specific expression.

17. In summary, the '648 specification specifically describes the sequence of SEQ ID NO:253 and the '648 specification specifically describes polynucleotides containing at least 50 contiguous nucleotides of SEQ ID NO:253. The '648 specification also specifically describes a wide variety of polynucleotides containing at least 50 contiguous nucleotides of SEQ ID NO:253 along with flanking sequences, e.g. probes, vectors, cDNAs, clones, full length cDNAs, genes etc. As such the '648 specification describes large polynucleotides containing fragments of SEQ ID NO:253 that are, for example, useful as probes or starting materials for probes (see, e.g., page 5, lines 7-14 of the '648 specification). The vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 and having such flanking sequences. The overall disclosure of the specification demonstrates that there is no criticality to sequences flanking the polynucleotides of the Invention. Rather, selection of such

flanking sequences is an arbitrary matter of design. The Skilled Person would readily appreciate from the specification that the sequence of SEQ ID NO:253 can be incorporated within a vast number of larger polynucleotides, and that each of these sequences is identifiable as having at least 50 contiguous nucleotides of SEQ ID NO:253.

18. When read in conjunction with the '648 specification, it is my unequivocal opinion that, a Skilled Person would find that the '648 specification describes polynucleotides fully representative of the genus of polynucleotides of the Invention since

a) the Skilled Person would recognize disclosure of SEQ ID NO:253 as fully representative of the genus of the Invention since it is a complete disclosure of the common structural feature (i.e., at least 50 contiguous nucleotides of SEQ ID NO:253) of the Inventions; and

b) the Skilled Person would recognize the vector containing a cDNA containing the sequence of SEQ ID NO:253 and deposited with the A.T.C.C. is an example of a polynucleotide containing SEQ ID NO:253 having flanking sequences and as being fully representative of large polynucleotides that can serve as probes or starting materials for probes in cancer diagnostics.

19. Based upon the above, the Skilled Person would conclude that the specification substantially and in detail describes the genus of polynucleotides encompassed in these claims 146-148. It is therefore my unequivocal opinion that a Skilled Person would, in March 2000, thus would find a clear and unambiguous description of the Inventions in Claims 146-148. Based on the foregoing, it is also my unequivocal opinion that a Skilled Person would find that the '648 specification demonstrates that applicants had possession of the genera of polynucleotides of claims 146-148.

20. Furthermore, a Skilled Person, by performing a simple sequence comparison, e.g. a pairwise "BESTFIT" alignment between SEQ ID NO:253 and any given nucleotide would have been able to straightforwardly determine whether a given polynucleotide fell within any one of the claims: the given polynucleotide either has 50 nucleotides of sequence identity with SEQ ID NO:253 or it does not.

Claims 149-150

21. I shall now address the Invention of Claims 149-150. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion. .

22. Page 6 lines 2-28 of the specification describes a genus of polynucleotides that hybridize under stringent conditions to a polynucleotide having a sequence provided by the sequence listing:

> The polynucleotides of the invention also include polynucleotides having sequence similarity or sequence identity. Nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, *e.g.*, U.S. Patent No. 5,707,829.

23. The specification, on page 6 line 28 to page 7 line 3 further describes that the Inventions may be allelic variants, cDNAs or genes, and may be from a variety of species, including humans.

> Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.* allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences ("SEQ ID NOS:1-5252") under stringent hybridization

> conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related genes. The source of homologous genes can be any species, *e.g.* primate species, particularly human; rodents, such as rats and mice; canines, felines, bovines, ovines, equines, yeast, nematodes, etc.
>
> Preferably, hybridization is performed using at least 15 contiguous nucleotides of at least one of "SEQ ID NOS:1-5252." That is, when at least 15 contiguous nucleotides of one of the disclosed SEQ ID NOs. is used as a probe, the probe will preferentially hybridize with a gene or mRNA (of the biological material) comprising the complementary sequence, allowing the identification and retrieval of the nucleic acids of the biological material that uniquely hybridize to the selected probe. Probes from more than one SEQ ID NO. will hybridize with the same gene or mRNA if the cDNA from which they were derived corresponds to one mRNA. Probes of more than 15 nucleotides can be used, but 15 nucleotides represents enough sequence for unique identification.

24. It is well established that, in order to hybridize, two polynucleotides must share a definable structural characteristic: a region of significant sequence identity. The structural characteristic that defines the claimed genus is SEQ ID NO:253, to which members of the group hybridize under stringent conditions. Some of the polynucleotides encompassed by the claim may be longer than the sequence of SEQ ID NO:253 and contain flanking sequences, however, since they must be able to hybridize with a specified polynucleotide they must have sequences that are similar to the sequence of the specified polynucleotide, and thus are limited in structure by this requirement. As such, the structural characteristic defining this genus of claimed sequences is the sequence of SEQ ID NO:253.

25. I have also reviewed the U.S. Patent & Trademark Office's "Synopsis of Application of Written Description Guidelines,", as posted to the U.S.P.T.O world wide website on March 1, 2000 and I agree with the assertion that "a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claim because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs", as recited on page 36. I also agree with the

Synopsis of Application of Written Description Guidelines in that a recitation of "hybridization" in a claim imposes a structural limitation onto the claimed Inventions.

26. It is therefore my unequivocal opinion that a Skilled Person would, in March 2000, have found the specific description of the claimed genus of polynucleotides in the specification to be a sufficient structural description of the claimed Inventions and to demonstrate applicants had possession of the Invention of Claims 149 or 150.

27. Furthermore, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within Claims 149 or 150 by performing a straightforward stringent hybridization experiment, or by calculating the Tm of the a hybrid polynucleotide molecule under certain hybridization conditions using the well known equation provided by Sambrook et al (Molecular Cloning: A Laboratory Manual, CSHL Press, 1989).

"Tm = 81.5 + 1.6(log10[Na+]) + 0.41(fraction G + C)
– 0.63(% formamide) – (600/length of probe)"

Claim 151

28. I will now discuss the Invention of Claim 151. In addition to the above-described portions of the specification and information known to the Skilled Person, I rely on the following in forming my opinion.

29. Table 1 of the '648 application describes biological deposits which include vectors containing an insert, which insert contains the sequences described in the application. Table 1 indicates that a clone encompassing the sequence of SEQ ID NO:253 is deposited as clone M00001448D:C09 of Deposit Number 207068at the ATCC.

30. SEQ ID NO:253 represents a part of the nucleotide sequence contained within the insert of the deposited clone, and, as such, the deposited clone contains an

polynucleotide insert that is longer than SEQ ID NO:253 and contains flanking sequences. Since the deposited clone is from a library made from mRNA, the flanking sequence are cDNA flanking sequences.

31. Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claim 151 and recognize that the inventors were in possession of that Invention.

Claims 152-154

32. I will now discuss the Invention of Claims 152-154. In addition to the above-described portions of the specification and other information known to the Skilled Person, I rely on the following in forming my opinion.

33. Amplification is a process for synthesizing a nucleic acid enzymatically. To perform amplification, at least one oligonucleotide probe (i.e. a primer of a defined sequence) hybridizes with (i.e. base pairs to) a template nucleic acid (i.e., the starting material), and the probe is enzymatically extended to form a copy of one strand of the nucleic acid. Subsequent extension steps amplify both strands of the nucleic acid to form a duplex nucleic acid product that contains at least the probe binding site. Probe binding sites are usually at least 12-15 nucleic acids in length, and, as such, both the amplification product and the probes share a sequence of at least 12-15 nucleotides.

34. Amplification strategies, such as the polymerase chain reaction (PCR), lockdown PCR, and rapid amplification of cDNA ends (RACE) were well understood and practiced a Skilled Person in March 2000 (e.g. as described by the laboratory manuals Ausubel et al. (*Short Protocols in Molecular Biology*, 3rd ed., Wiley & Sons, 1995 and Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Second Edition,

1989 Cold Spring Harbor, N.Y.). In many amplification strategies, such as RACE and lockdown PCR, nucleotide sequences flanking a sequence of interest may be amplified. In the specification, several amplification strategies are detailed, such as PCR, lockdown PCR and RACE. In most PCR methods, probes are first designed, and the PCR is performed. The specification provides description of a SEQ ID NO:253, a description of probes, and a description of PCR methods as follows:

35. SEQ ID NO:253 is described in the sequence listing submitted as part of the application, as recited in paragraph 11, *supra*.

36. Probe sequences are detailed in the specification on page 9, lines 15-18:

> Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in "SEQ ID NOS:1-5252." The probes are preferably at least about 12, 15, 16, 18, 20, 22, 24, or 25 nucleotide fragment of a corresponding contiguous sequence of "SEQ ID NOS:1-5252",

37. Polymerase Chain Reaction (PCR) is detailed in the specification at page 37, lines 1-6.

> The Polymerase Chain Reaction (PCR) is another means for detecting small amounts of target nucleic acids (see, *e.g.*, Mullis *et al.*, *Meth. Enzymol.* (1987) *155*:335; U.S. Patent No. 4,683,195; and U.S. Patent No. 4,683,202). Two primer polynucleotides nucleotides hybridize with the target nucleic acids and are used to prime the reaction. The primers can be composed of sequence within or 3' and 5' to the polynucleotides of the Sequence Listing.

38. On page 13, lines 4-15, RACE is described:

> "Rapid amplification of cDNA ends," or RACE, is a PCR method of amplifying cDNAs from a number of different RNAs. The cDNAs are ligated to an oligonucleotide linker, and amplified by PCR using two primers. One primer is based on sequence from the instant polynucleotides, for which full length sequence is desired, and a

> second primer comprises sequence that hybridizes to the oligonucleotide linker to amplify the cDNA. A description of this methods is reported in WO 97/19110. In preferred embodiments of RACE, a common primer is designed to anneal to an arbitrary adaptor sequence ligated to cDNA ends (Apte and Siebert, *Biotechniques* (1993) *15*:890-893; Edwards *et al.*, *Nuc. Acids Res.* (1991) *19*:5227-5232). When a single gene-specific RACE primer is paired with the common primer, preferential amplification of sequences between the single gene specific primer and the common primer occurs. Commercial cDNA pools modified for use in RACE are available.

39. On page 13, lines 16-18, an anchored PCR strategy is described:

> Another PCR-based method generates full-length cDNA library with anchored ends without needing specific knowledge of the cDNA sequence. This method is described in WO 96/40998.

40. In summary, the specification specifically describes SEQ ID NO:253, the specification specifically describes that oligonucleotide probes for use in amplification can be at least 15 contiguous nucleotides of an SEQ ID NO:253, and the specification specifically describes starting material for use in the amplification process, as well as the polynucleotides that would be produced by amplification using the probes and the starting material. These polynucleotides share the structural feature of at least 50 contiguous nucleotides of SEQ ID NO:253.

41. Based upon the above disclosures in the '648 application, it is my unequivocal opinion that a Skilled Person would find that the '648 application describes the Invention of Claims 152-154 and recognize that the inventors were in possession of that Invention

The Office Actions

42. I have been asked to comment on the Office Actions, including the first Office Action (specifically section No. 7) mailed November 29, 2000 and the final Office Action (specifically section No. 12) mailed October 2, 2001.

43. It is my understanding that the positions outlined in these Office Actions were taken with respect to other claimed Inventions, and that the same reasoning might be applied to the new claims directed to these Inventions.

44. As I understand it, claims directed to the above-described Inventions have been rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the Inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action argues that the specification provides insufficient written description to support the genus of nucleic acid sequences encompassed by the claims, which include sequences longer than SEQ ID NO:253 and sequences that hybridize to SEQ ID NO:253. The Office Actions further asserts that with the exception of a polynucleotide that is limited to at least 50 contiguous nucleotides of SEQ ID NO:253 and no more, one of ordinary skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Based on my knowledge of the Skilled Person, I disagree with this statement.

45. As I have discussed above, the sequence of SEQ ID NO:253 defines structural features commonly possessed by members of each of the genera of the Inventions that distinguish them from other polynucleotides. SEQ ID NO:253 thus defines the claimed genera of polynucleotides such that a Skilled Person would have recognized that the inventors had possession of and had invented the claimed polynucleotides.

Moreover, the Skilled Person would have been able to straightforwardly determine whether a given polynucleotide falls within any one of the claims based on the provided structural characteristics or routine hybridization experiments. Only routine methodologies would be required to determine whether a given polynucleotide would be within a genus of an Invention. The specification provides, therefore, sufficient written description of the characterizing details sufficient to distinguish the claimed genera of polynucleotides from all others, which means the genera are readily recognizable by the Skilled Person.

46. Furthermore, in reviewing the Office Actions, I note that the written description rejection cites the following court decisions in support of the rejection: *Amgen, Inc. v. Chugai Pharmaceutical Co.*, *Fiers v. Revel*, *Fiddes v. Baird*, and *University of California v. Eli Lilly and Co.* I understand that the disputed patent applications were filed in the between the late 1970's and the mid-1980s.

47. Since the field of recombinant DNA technology is a rapidly evolving, and most major technological advances have been made in the last 20 years (e.g. computer programs for comparing nucleic acids), a Skilled Person had a dramatically higher skill level in March 2000 as compared to the filing dates of the applications involved in the above court decisions. As I understand it, the written description requirement is evaluated in the context of the person of ordinary skill in the art at the time of filing. Because of the advances in the art, I do not believe that a statement regarding what one of ordinary skill can or cannot do in the above cases could be evidence with respect to what the Skilled Person in March of 2000 could or could not do.

48. I, Christopher R. Somerville, hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

11-1-02
Date

Christopher R. Somerville
Christopher R. Somerville, Ph.D.

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